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Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System

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There is no additional data available for this manuscript.

Abstract:

Objectives: to describe the clinical profile of Brazilian type 2 diabetic patients attending the public healthcare system and identify factors associated with poor glycemic control.

Design: Cross-sectional study.

Setting: 14 centers in five regions of Brazil, including primary care units and outpatient clinics of University Hospitals.

Participants: Patients with type 2 diabetes attending outpatient clinics of public health care system.

Main Outcome Measured: HbA1c, centrally measured by HPLC (NGSP certified).

Results: A total of 5,750 patients aged 61±10 years, with 11±8 years of diabetes duration (66% female, 56% non-white, BMI: 28.0±5.3 kg/m²) were analyzed. Mean HbA1c was 8.6±2.2%, and median HbA1c was 8.1% (6.9 to 9.9%). HbA1c <7% was observed in only 26% of patients. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast (8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South regions (8.3±1.9%). Using the cutoff value of HbA1c above the median, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)], and being from Midwest region [0.858 (0.745-0.989)] were protective factors, while diabetes duration [1.015 (1.012-1.018)], use of insulin [1.710 (1.624-1.802)], and living in the Northeast region [1.197 (1.085-1.321)] were associated with HbA1c >8%.

Conclusions: The majority of Brazilian type 2 diabetic patients attending the public healthcare system had HbA1c levels above recommended targets. The recognition of Northeast residents and non-white patients as vulnerable populations should guide future policies and actions to prevent and control diabetes.

Introduction

Brazil is among the ten countries with the highest prevalence of diabetes mellitus (DM) in the world – about 7.6% (1,2). Diabetes is the fifth underlying cause of death in Brazil, affecting 2.5% of the population (3). Preliminary results obtained by our group (4) show that only 24% of Brazilian diabetic patients had an HbA1c level below the recommended target (HbA1c <7%; 5), despite the availability of free medical care through the public healthcare system (Sistema Único de Saúde-SUS) (6). Medical assistance–and specific drugs, including metformin, sulphonylureas, and insulin, are provided free of charge across the country through primary care units and specific drugstores. Considering that poor diabetic control is associated with increased mortality in diabetic populations (7), it is important to analyze the possible factors associated with the high levels of HbA1c in the population.

Therefore, the aim of this study was to describe the clinical profile of patients with type 2 diabetes receiving public health care in the five regions of Brazil and identify factors associated with poor glycemic control.

Patients

A cross-sectional study was conducted between February 2006 and April 2011 at SUS outpatient clinics with 7,201 type 1 and type 2 diabetes patients from the North (n = 500; 7%), Northeast (n = 2184; 30%), Midwest (n = 461; 6%), Southeast (n = 3382; 47%), and South (n = 674; 9%) regions of Brazil. The number of patients in each region reflects the regional population density as reported in the 2000 national census (8). A preliminary report describing the characteristics of this patient population, for all regions except the North, has been published (4). The protocol was approved by the

Ethics Committee at Hospital de Clínicas de Porto Alegre and at each participating center/clinic. All patients provided written informed consent.

In the present study, we report the results for 5,750 type 2 diabetic patients for whom HbA1c values were available. Type 2 diabetes was defined as diabetes diagnosed after 30 years of age without insulin use in the first five years after the diagnosis. Patients were from the North (n = 312; 5%), Northeast (n = 1906, 33%), Midwest (n = 348, 6%), Southeast (n = 2642, 46%), and South (n = 542, 9%) regions.

Assessment of Clinical Characteristics

Information on clinical variables (age, gender, ethnicity, DM duration, body weight, height, physical activity, and medications in use,) was obtained by a standardized questionnaire. Ethnicity was self-reported as white or non-white (black, mixed, or other – including Asian and Native Brazilians). Marital status was categorized as living with or without a partner, and working status as being or not currently employed. Educational status was classified as at least eight years or less than eight years of formal education. DM treatment was classified as none, diet alone, oral agents, oral agents plus insulin, and insulin alone. Frequency of self-blood glucose monitoring (SBGM) and hypoglycemic episodes in the previous year were recorded. BMI was calculated (weight/height^2; kg/m^2). Data were collected in 14 cities representing the 5 regions of Brazil: South (Porto Alegre, Curitiba), Southeast (São Paulo, Cotia, Campinas, Belo Horizonte, Rio de Janeiro), Midwest (Brasilia, Taguatinga), Northeast (Fortaleza, Recife, Salvador), North (Belém, Manaus).

HbA1c measurements

HbA1c was measured in a central laboratory by an ion-exchange high performance liquid chromatography (HPLC) method (reference range 4.7-6.0%)

certified by the National Glycohemoglobin Standardization Program (NGSP) and calibrated to the Diabetes Control and Complications Trial (DCCT) standard.

Statistical Analyses

The five regions were compared in terms of clinical variables and HbA1c results by one-way-ANOVA (with Bonferroni post-hoc test) and chi-square tests. The characteristics of patients were evaluated according to glucose control (median HBA1c), region of origin, and self-reported ethnic background. Prevalence ratio (PR) and 95% confidence interval were obtained by Poisson regression analyses to determine the association of different factors with HbA1c >8% (dependent variable). Adjustment was made taking into account independent variables selected based on their significance on univariate analyses and/or biological relevance.

Variables were expressed as mean ± SD, number of cases (%) and median (25-75 interquartile intervals). HbA1c was also described as median. Statistical analyses were carried out using SSPS 18.0. P values less than 0.05 (two tailed) were considered significant.

RESULTS

A total of 5,750 patients with type 2 diabetes were included and the main characteristics were: age of 61±10 years, diabetes duration of 11±8 years, and BMI 28.0 ±5.3 kg/m^2. Most patients were female (66%), non-white (56%), and lived with a partner (59%). One third (33%) had completed eight years of formal education, 20% were employed and 37% were not physically active. Regarding treatment, 1% did not follow any kind of treatment for diabetes, 6% were on diet alone, 57% were taking oral agents, 22% used oral agents and insulin and 13% insulin alone. Mean HbA1c was 8.6

±2.2% and median was 8.1% (interquartile range: 6.9 to 9.9%). HbA1c <7% was found in only 26% of the patients.

Since the majority of the included patients had a poor glycemic control we decided to compare the characteristic of patients grouped according to median HbA1c (8.0%). **Table 1** describes clinical characteristics and prevalence ratio [PR (CI95%)] of patients with HbA1c ≥8% and HbA1c<8%. In unadjusted model, patients with HbA1c ≥8% were younger, non-whites, with longer DM duration, more sedentary, mainly from North and Northeast regions and treated more frequently with insulin than patients with HbA1c <8%. After adjustment, DM duration [1.015 (1.012-1.018)], insulin use [1.710 (1.624-1.802)], and being from Northeast region [1.197 (1.085-1.321)] was associated with HbA1c ≥8%. On the other hand, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)] and living in the Midwest region (using the South region as reference) [0.858 (0.745-0.989)] were protective factors. In order to further explore the variables associated with HbA1c ≥8% we performed stratified analysis according to geographic region, ethnicity and insulin use.

The characteristics of the patients stratified by region are described in **Table 2**. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast (8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South (8.3±1.9%) regions. Moreover, the five regions differed in all other evaluated characteristics. Patients living in the Northeast had the highest prevalence of non-whites, the lowest BMI, and the highest frequency of employed individuals.

Characteristics of patients according self-reported ethnicity (white and non-white) are described in **Table 3**. Non-white subjects had higher HbA1c values, lower BMI, and more years of formal education than white patients. They were also younger, more often female and single.

Of the 5,750 patients in this study, 35% (2,021 patients) used insulin. Of these, 33% (n = 658) used insulin once daily, 58% (n = 1,154) twice daily, and 9% (n = 189) three times a day or more. Eighty-one percent (n = 1,630) of the insulin users performed SBGM, but only 421 (26%) did it on a daily basis. Patients who performed more frequently SBGM had lower values of HbA1c (at least once daily: 9.3 ± 2.1%) than who did not measure capillary glucose (9.7 ± 2.3%; P = 0.008).

Conclusions

In this study, most patients with type 2 diabetes attending the public healthcare system in Brazil had HbA1c levels above the recommended target, that is, above 7%. Being non-white and from the Northeast, as well as the longer diabetes duration, and insulin use were factors associated with poor metabolic control, whereas age and being from the Midwest were associated with HbA1c <8.0% (median HbA1c level for this population). To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil. By including patients from the five regions of the country and using a certified method to measure the main outcome, HbA1c level, we were also able to produce a representative profile of the population of type 2 diabetic patients attending the public healthcare system in Brazil.

Diabetes control varies in different countries. In the Unites States of America, mean HbA1c among middle-aged adults was approximately 7.3% (9). Type 2 diabetic patients using oral agents to treat diabetes in seven European countries had similar glycemic control (mean HbA1c 7.2%) (10). However, in the EURIKA (11), a study performed in 12 European countries, only 36.7% of patients with type 2 diabetes achieved the goal of HbA1c <6.5%. In the present study, mean HbA1c (8.6±2.2%) was much higher than that observed in these countries, and only 26% of our patients had HbA1c below the 7.0% goal.

In our study, a broad range of HbA1c levels was also observed across Brazilian regions. The poorer glycemic control observed in the Northeast than the other regions might be explained by a diverse ethnic and economic background. Numerous studies show ethnic disparities in HbA1c values; a meta-analysis has reported that African-Americans had absolute HbA1c values 0.65% higher than non-Hispanic whites (13). According to the Brazilian Geography and Statistics Institute, 23.6% of the population in the North and 28.9% in Northeast are white, vs. 41.7% in the Midwest, 56.7% in the Southeast, and 78.5% in the South (12). In our study, the difference in HbA1c between whites and non-whites was about 0.5%. Regarding the role of economic status, *per capita* income is almost twice as high in the South than in the Northeast (14). In this sense, a European surveillance of socio-economic predictors of mortality has demonstrated an association between low income (15) and higher mortality in type 2 diabetic males.

Free, universal health care has been available to all Brazilian citizens since 1988-(6), including free access to many drugs. Metformin, sulphonylureas, and insulin are distributed in primary care units and drugstores around the country. However, other medications used to treat diabetes are not covered. Also, SBGM devices are not freely supplied. Therefore, although our Public Health System may represent an advance in health care, it has not been enough to reach glycemic control targets in diabetes care. Other measures are highly necessary, and should include a structured diabetes education program (16), public policies to improve adherence to diet and exercise, and free access to SBGM, at least to all patients on insulin (5).

The present study has limitations. Firstly, surveillance was based on self-reported answers, although medical records were consulted when available. Moreover, only patients attending the public healthcare system were evaluated. It is known that

almost one fourth of the Brazilian population rely on private healthcare (17). Lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors. It is also important to remember that reverse causality is always possible in cross-sectional studies, and poor glycemic control in patients using insulin cannot be attributed to insulin prescription *per se*. Because insulin is generally prescribed to patients with more severe diabetes, the health status of these patients may also account for their poor glycemic control.

In conclusion, Brazilian patients with type 2 diabetes attending the public healthcare system have poor glycemic control as demonstrated by HbA1c values far above the recommended target. New strategies are necessary to improve glycemic control in this population. Furthermore, the increased vulnerability of Northeast residents and non-white patients to poor metabolic control should be taken into account when designing strategies to control diabetes.

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Table 1 . Prevalence of patients characteristics according to HbA1c ≥8%

	HbA1c <8% n = 2791	HbA1c ≥8% n = 2959	PR (CI 95%)	P	Adjusted PR (CI95%)	P
Age (years)	62 ± 11	60 ± 10	0.991 (0.989-0.993)	0.000	0.986 (0.983-0.989)	0.000
Diabetes duration (years)	9 ± 8	12 ± 8	1.018 (1.015-1.021)	0.000	1.015 (1.012-1.018)	0.000
BMI (kg/m²)	28.0 ± 5.1	28. 0 ± 5.4	0.999 (0.994-1.004)	0.640	--	--
Females	1824 (65)	1972 (67)	0.972 (0.922-1.026)	0.304	--	--
White	1339 (48)	1199 (40)	0.862 (0.818-0.907)	0.000	0.931 (0.883-0.981)	0.007
Living with a partner	1613 (58)	1762 (59)	1.035 (0.983-1.089)	0.189	1.006 (0.959-1.057)	0.796
≥ 8 years of formal education	933 (41)	967 (48)	0.987 (0.932-1.044)	0.646	--	--
Active worker	527 (19)	609 (21)	0.949 (0.893-1.009)	0.094	1.053 (0.989-1.212)	0.109
Ever participate in a diabetes education program*	318 (11)	387 (13)	0.929 (0.865-0.999)	0.047	--	--
Diabetes treatment				0.000	--	--
None	48 (2)	23 (1)				
Diet only	285 (10)	58 (2)	0.522 (0.346-0.786)			
Oral agents	1905 (69)	1390 (47)	1.302 (0.928-1.827)			
Oral agents and insulin	318 (11)	930 (32)	2.300 (1.641-3.224)			
Insulin alone	228 (8)	545 (18)	2.176 (1.551-3.055)			

Insulin use	546 (20)	1475 (50)	1.834 (1.749-1.924)	0.000	1.710 (1.624-1.802)	0.000
SBMG	1,838 (66)	2158 (73)	1.186 (1.118-1.1258)	0.000	1.061(1.001-1.1.23)	0.045
Geographic region				0.000		0.000
North	135 (43)	177 (57)	1.225 (1.073-1.399)		1.137 (0.996-1.298)	
Northeast	814 (43)	1092 (57)	1.212 (1.212-1.365)		1.197 (1.085-1.321)	
Midwest	194 (56)	154 (44)	0.956 (0.842-1.109)		0.858 (0.745-0.989)	
Southeast	1,357 (51)	1285 (49)	1.050 (0.951-1.159)		0.959 (0.871-1.056)	
South	291 (54)	251 (46)				

*Data not available for North region (not included in the adjusted analysis)

Table 2. Characteristics of patients with type 2 diabetes according to the five geographic regions of Brazil

	North	Northeast	Midwest	Southeast	South	P
N	312	1906	348	2642	542	-
HbA1c (%)	9.0 ± 2.6	8.9 ± 2.4	8.1 ± 2.0	8.4 ± 2.1	8.3 ± 1.9	<0.01[a]
Age (years)	58 ± 10	61 ± 11	60 ± 11	61 ± 10	62 ± 10	<0.01[bc]
Diabetes duration (years)	10 ± 8	10 ± 8	11 ± 8	11 ± 9	11 ± 9	0.029
BMI (kg/m²)	29.0 ± 5.5	27.2 ± 5.0	27.7 ± 5.2	28.2 ± 5.3	29.1 ± 5.3	<0.01[cde]
Females	193 (62)	1,317 (69)	245 (70)	1,726 (65)	315 (58)	<0.01[f]
White	71 (23)	560 (29)	131 (38)	1,311 (50)	465 (86)	<0.01[f]
Living with a partner	199 (64)	1,099 (58)	185 (53)	1,537 (58)	355 (66)	<0.01[g]
≥ 8 years of formal education	140 (45)	521 (34)	106 (39)	1,011 (38)	122 (27)	<0.01[h]
Active worker	112 (38)	341 (18)	65 (19)	482 (18)	136 (25)	<0.01[i]
Sedentary	134 (43)	670 (35)	147 (43)	1,005 (38)	168 (31)	<0.01[j]
Diabetes treatment						
None	2 (1)	18 (1)	7 (2)	38 (1)	6 (1)	<0.01[f]
Diet only	14 (5)	145 (8)	31 (9)	138 (5)	15 (3)	
Oral agents	172 (59)	1172 (62)	180 (52)	1,426 (54)	345 (64)	
Oral agents and insulin	67 (23)	332 (17)	64 (18)	660 (25)	125 (23)	
Insulin alone	37 (12)	239 (12)	66 (19)	380 (15)	51 (9)	

Data are mean ± SD or number of patients with the characteristic (%)

[a] North and Northeast vs. Midwest, Southeast and South

[b] North vs. Northeast, Southeast and South

[c] Midwest and Southeast vs. South

[d] North vs. Northeast and Center-West

[e] Northeast vs. Southeast and South

[f] Linear-by-linear association

[g] higher in North and South; lower in Midwest

[h] higher in North; lower in Northeast and South

[i] higher in North and South; lower in Northeast and Southeast

[j] higher in North and Midwest; lower in Northeast and South

Table 3. Demographic and clinical characteristics of patients with type 2 diabetes according to ethnicity

	White n = 2538	Non-white n = 3208	P
HbA1c (%)	8.3 ± 2.1	8.8 ± 2.3	<0.01
Age (years)	62 ± 10	60 ± 10	<0.01
Diabetes duration (years)	11 ± 9	11 ± 8	0.06
BMI (kg/m²)	28.2 ± 5.2	27.8 ± 5.3	0.003
Females – n (%)	1,615 (64)	2,178 (68)	<0.01
Living with a partner - n (%)	1,568 (62)	1,805 (56)	<0.01
At least eight years of formal education - n (%)	803 (38)	1,094 (41)	0.011
Active worker - n (%)	520 (21)	616 (19)	0.227
Sedentary – n (%)	904 (36)	1,220 (38)	0.072
Diabetes treatment - n (%)			0.007
None	37 (2)	34 (1)	
Diet only	151 (6)	192 (6)	
Oral agents	1,498 (59)	1,794 (56)	
Oral agents and insulin	533 (21)	714 (22)	
Insulin alone	314 (12)	459 (15)	
Geographic region – n (%)			<0.01
North	71 (23)	241 (77)	
Northeast	560 (29)	1,344 (71)	
Midwest	131 (38)	217 (62)	
Southeast	1,311 (50)	1,329 (50)	
South	465 (86)	77 (14)	

Data are mean ± SD, number of patients with the characteristic (%)

Figure 1. HbA1c Distribution Among the Five Brazilian Geographic Regions. (HbA1c higher in the North and Northeast regions vs South, Southeast, and Midwest Regions P<0.01).

Summary

Article Focus:

Brazil is among the ten countries in the world with the highest prevalence of diabetes mellitus (DM). It is a large country with marked ethnic and socioeconomic differences between regions. Free, universal healthcare coverage is available to all Brazilians, including free access to many drugs. However, status of diabetes control in Brazil is unknown.

Key Messagens:

Patients with type 2 diabetes attending public health care system in Brazil had a mean HbA1c of 8.6%, above recommended international goals. Non-whites and patients living in the Northeast region of the country had the poorest glycemic control. This vulnerable population should receive special attention from government health policies.

Strengths and Limitations

To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil. We used a certified method to analyse HbA1c. However, some limitations were: 1) surveillance was based on self-reported answers, although medical records were consulted when available. 2) Only patients attended by the public heath system were included and 3) lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract OK
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found OK
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported OK
Objectives	3	State specific objectives, including any prespecified hypotheses OK
Methods		
Study design	4	Present key elements of study design early in the paper OK
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection OK
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants OK
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group OK
Bias	9	Describe any efforts to address potential sources of bias OK
Study size	10	Explain how the study size was arrived at OK
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why OK
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding OK
		(*b*) Describe any methods used to examine subgroups and interactions OK
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed OK
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders OK
		(b) Indicate number of participants with missing data for each variable of interest OK
Outcome data	15*	Report numbers of outcome events or summary measures OK
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and

		their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included OK
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives OK
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias OK
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence OK
Generalisability	21	Discuss the generalisability (external validity) of the study results OK
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based OK

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System

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Factors Associated with Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System

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There is no additional data available for this manuscript.

Abstract:

Objectives: to describe the clinical profile of Brazilian type 2 diabetic patients attending the public healthcare system and identify factors associated with poor glycemic control.

Design: Cross-sectional study.

Setting: 14 centers in five regions of Brazil, including primary care units and outpatient clinics of University Hospitals.

Participants: Patients with type 2 diabetes attending outpatient clinics of public health care system.

Main Outcome Measured: HbA1c, centrally measured by HPLC (NGSP certified).

Results: A total of 5,750 patients aged 61±10 years, with 11±8 years of diabetes duration (66% female, 56% non-white, BMI: 28.0±5.3 kg/m²) were analyzed. Mean HbA1c was 8.6±2.2%, and median HbA1c was 8.1% (6.9 to 9.9%). HbA1c <7% was observed in only 26% of patients. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast (8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South regions (8.3±1.9%). Using the cutoff value of HbA1c above the median, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)], and being from Midwest region [0.858 (0.745-0.989)] were protective factors, while diabetes duration [1.015 (1.012-1.018)], use of insulin [1.710 (1.624-1.802)], and living in the Northeast region [1.197 (1.085-1.321)] were associated with HbA1c >8%.

Conclusions: The majority of Brazilian type 2 diabetic patients attending the public healthcare system had HbA1c levels above recommended targets. The recognition of Northeast residents and non-white patients as vulnerable populations should guide future policies and actions to prevent and control diabetes.

Introduction

Brazil is among the ten countries with the highest prevalence of diabetes mellitus (DM) in the world – about 7.6% (1,2). Diabetes is the fifth underlying cause of death in Brazil, affecting 2.5% of the population (3). Preliminary results obtained by our group (4) show that only 24% of Brazilian diabetic patients had an HbA1c level below the recommended target (HbA1c <7%; 5), despite the availability of free medical care through the public healthcare system (Sistema Único de Saúde-SUS) (6). Medical assistance–and specific drugs, including metformin, sulphonylureas, and insulin, are provided free of charge across the country through primary care units and specific drugstores. Considering that poor diabetic control is associated with increased mortality in diabetic populations (7), it is important to analyze the possible factors associated with the high levels of HbA1c in the population.

Therefore, the aim of this study was to describe the clinical profile of patients with type 2 diabetes receiving public health care in the five regions of Brazil and identify factors associated with poor glycemic control.

Patients

A cross-sectional study was conducted between February 2006 and April 2011 at SUS outpatient clinics with 7,201 type 1 and type 2 diabetes patients from the North (n = 500; 7%), Northeast (n = 2184; 30%), Midwest (n = 461; 6%), Southeast (n = 3382; 47%), and South (n = 674; 9%) regions of Brazil. The number of patients in each region reflects the regional population density as reported in the 2000 national census (8). A preliminary report describing the characteristics of this patient population, for all regions except the North, has been published (4). Briefly, the current study was designed to obtain a representative sample of type 2 diabetic adult patients living in urban areas of Brazil. A total of 14 centers, located in 12 cities belonging to the five

regions of our country were included. The included cities were the largest in their respective region and nine of them ranked among the most populous municipalities in Brazil. We also considered that the data would be more reliable if they were collected from public health care centers that usually take care of at least three hundreds diabetic patients/month. The protocol was approved by the Ethics Committee at Hospital de Clínicas de Porto Alegre and at each participating center/clinic. All patients provided written informed consent.

In the present study, we report the results for 5,750 type 2 diabetic patients for whom HbA1c values were available. Type 2 diabetes was defined as diabetes diagnosed after 30 years of age without insulin use in the first five years after the diagnosis. Patients were from the North (n = 312; 5%), Northeast (n = 1906, 33%), Midwest (n = 348, 6%), Southeast (n = 2642, 46%), and South (n = 542, 9%) regions.

Assessment of Clinical Characteristics

Information on clinical variables (age, gender, ethnicity, DM duration, body weight, height, physical activity, and medications in use,) was obtained by a standardized questionnaire. Ethnicity was self-reported as white or non-white (black, mixed, or other – including Asian and Native Brazilians). Marital status was categorized as living with or without a partner, and working status as being or not currently employed. Educational status was classified as at least eight years or less than eight years of formal education. DM treatment was classified as none, diet alone, oral agents, oral agents plus insulin, and insulin alone. Frequency of self-blood glucose monitoring (SBGM) and hypoglycemic episodes in the previous year were recorded. BMI was calculated (weight/height^2; kg/m^2). Data were collected in 14 cities representing the 5 regions of Brazil: South (Porto Alegre, Curitiba), Southeast (São Paulo, Cotia,

Campinas, Belo Horizonte, Rio de Janeiro), Midwest (Brasilia, Taguatinga), Northeast (Fortaleza, Recife, Salvador), North (Belém, Manaus).

HbA1c measurements

HbA1c was measured in a central laboratory by an ion-exchange high performance liquid chromatography (HPLC) method (reference range 4.7-6.0%) certified by the National Glycohemoglobin Standardization Program (NGSP) and calibrated to the Diabetes Control and Complications Trial (DCCT) standard.

Statistical Analyses

The five regions were compared in terms of clinical variables and HbA1c results by one-way-ANOVA (with Bonferroni post-hoc test) and chi-square tests. The characteristics of patients were evaluated according to glucose control (median HBA1c), region of origin, and self-reported ethnic background. Prevalence ratio (PR) and 95% confidence interval were obtained by Poisson regression analyses to determine the association of different factors with HbA1c >8% (dependent variable). Adjustment was made taking into account independent variables selected based on their significance on univariate analyses and/or biological relevance (age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG, and geographic region).

Variables were expressed as mean ± SD, number of cases (%) and median (25-75 interquartile intervals). HbA1c was also described as median. Statistical analyses were carried out using SSPS 18.0. P values less than 0.05 (two tailed) were considered significant.

RESULTS

A total of 5,750 patients with type 2 diabetes were included and the main characteristics were: age of 61±10 years, diabetes duration of 11±8 years, and BMI 28.0

±5.3 kg/m^2. Most patients were female (66%), non-white (56%), and lived with a partner (59%). One third (33%) had completed eight years of formal education, 20% were employed and 37% were not physically active. Regarding treatment, 1% did not follow any kind of treatment for diabetes, 6% were on diet alone, 57% were taking oral agents, 22% used oral agents and insulin and 13% insulin alone. Mean HbA1c was 8.6 ±2.2% and median was 8.1% (interquartile range: 6.9 to 9.9%). HbA1c <7% was found in only 26% of the patients.

Since the majority of the included patients had a poor glycemic control we decided to compare the characteristic of patients grouped according to median HbA1c (8.0%). **Table 1** describes clinical characteristics and prevalence ratio [PR (CI95%)] of patients with HbA1c ≥8% and HbA1c<8%. In unadjusted model, patients with HbA1c ≥8% were younger, non-whites, with longer DM duration, more sedentary, mainly from North and Northeast regions and treated more frequently with insulin than patients with HbA1c <8%. After adjustment, DM duration [1.015 (1.012-1.018)], insulin use [1.710 (1.624-1.802)], and being from Northeast region [1.197 (1.085-1.321)] was associated with HbA1c ≥8%. On the other hand, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)] and living in the Midwest region (using the South region as reference) [0.858 (0.745-0.989)] were protective factors. In order to further explore the variables associated with HbA1c ≥8% we performed stratified analysis according to geographic region, ethnicity and insulin use. A **Supplementary Table** shows unadjusted and adjusted analyses applying the same multivariate model using a cutoff of HbA1c<7%. The differences between the groups of patients with HbA1c <7% and ≥7% did not differ substantially from the results using the cutoff of HbA1c<8%.

The characteristics of the patients stratified by region are described in **Table 2**. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast

(8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South (8.3±1.9%) regions. Moreover, the five regions differed in all other evaluated characteristics. Patients living in the Northeast had the highest prevalence of non-whites, the lowest BMI, and the highest frequency of employed individuals.

Characteristics of patients according self-reported ethnicity (white and non-white) are described in **Table 3**. Non-white subjects had higher HbA1c values, lower BMI, and more years of formal education than white patients. They were also younger, more often female and single.

Of the 5,750 patients in this study, 35% (2,021 patients) used insulin. Of these, 33% (n = 658) used insulin once daily, 58% (n = 1,154) twice daily, and 9% (n = 189) three times a day or more. Eighty-one percent (n = 1,630) of the insulin users performed SBGM, but only 421 (26%) did it on a daily basis. Patients who performed more frequently SBGM had lower values of HbA1c (at least once daily: 9.3 ± 2.1%) than who did not measure capillary glucose (9.7 ± 2.3%; P = 0.008).

Conclusions

In this study, most patients with type 2 diabetes attending the public healthcare system in Brazil had HbA1c levels above the recommended target, that is, above 7%. Being non-white and from the Northeast, as well as the longer diabetes duration, and insulin use were factors associated with poor metabolic control, whereas age and being from the Midwest were associated with HbA1c <8.0% (median HbA1c level for this population). To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil using a certified method to measure HbA1c. We also may consider that the present study included a representative sample of patients with type 2 diabetes living in the urban areas and attending the public healthcare system in Brazil.

In the current survey we chose to use the cutoff value of HbA1c 8% to compare patients with different glycemic control. The recommended target for HbA1c is below 7%, but it has been recently recommended to individualize the goal of HbA1c (5). Since only 26% of our patients achieved this target, we adopted a more representative cutoff value (median HbA1c value of our study population). Nevertheless, we also performed an analysis using the cutoff of HbA1c<7% and the results did not change.

Diabetes control varies in different countries. In the Unites States of America, mean HbA1c among middle-aged adults was approximately 7.3% (9). Type 2 diabetic patients using oral agents to treat diabetes in seven European countries had similar glycemic control (mean HbA1c 7.2%) (10). However, in the EURIKA (11), a study performed in 12 European countries, only 36.7% of patients with type 2 diabetes achieved the goal of HbA1c <6.5%. In the present study, mean HbA1c (8.6±2.2%) was much higher than that observed in these countries, and only 26% of our patients had HbA1c below the 7.0% goal.

In our study, a broad range of HbA1c levels was also observed across Brazilian regions. The poorer glycemic control observed in the Northeast than the other regions might be explained by a diverse ethnic and economic background. Numerous studies show ethnic disparities in HbA1c values; a meta-analysis has reported that African-Americans had absolute HbA1c values 0.65% higher than non-Hispanic whites (13). According to the Brazilian Geography and Statistics Institute, 23.6% of the population in the North and 28.9% in Northeast are white, vs. 41.7% in the Midwest, 56.7% in the Southeast, and 78.5% in the South (12). In our study, the difference in HbA1c between whites and non-whites was about 0.5%. Regarding the role of economic status, *per capita* income is almost twice as high in the South than in the Northeast (14). In this sense, a European surveillance of socio-economic predictors of mortality has

demonstrated an association between low income (15) and higher mortality in type 2 diabetic males.

Free, universal health care has been available to all Brazilian citizens since 1988 (6), including free access to many drugs. Metformin, sulphonylureas, and insulin are distributed in primary care units and drugstores around the country. However, other medications used to treat diabetes are not covered. Also, SBGM devices are not freely supplied. Therefore, although our Public Health System may represent an advance in health care, it has not been enough to reach glycemic control targets in diabetes care. Other measures are highly necessary, and should include a structured diabetes education program (16), public policies to improve adherence to diet and exercise, and free access to SBGM, at least to all patients on insulin (5).

The present study has limitations. Firstly, surveillance was based on self-reported answers, although medical records were consulted when available. Moreover, only patients attending the public healthcare system were evaluated. It is known that almost one fourth of the Brazilian population rely on private healthcare (17). Lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors. It is also important to remember that reverse causality is always possible in cross-sectional studies, and poor glycemic control in patients using insulin cannot be attributed to insulin prescription *per se*. Because insulin is generally prescribed to patients with more severe diabetes, the health status of these patients may also account for their poor glycemic control. We may consider that had included only diabetic patients living in urban areas could represent a potential limitation. However we can speculate that patients from the rural areas of our country, who attend primary care units less equipped and with less trained health care personal, may have even a poorer diabetes control.

In conclusion, Brazilian patients with type 2 diabetes attending the public healthcare system have poor glycemic control as demonstrated by HbA1c values far above the recommended target. New strategies are necessary to improve glycemic control in this population. Furthermore, the increased vulnerability of Northeast residents and non-white patients to poor metabolic control should be taken into account when designing strategies to control diabetes.

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Table 1 . Prevalence of patients characteristics according to HbA1c ≥8%

	HbA1c <8% n = 2791	HbA1c ≥8% n = 2959	PR (CI 95%)	P	Adjusted PR (CI95%) *	P
Age (years)	62 ± 11	60 ± 10	0.991 (0.989-0.993)	0.000	0.986 (0.983-0.989)	0.000
Diabetes duration (years)	9 ± 8	12 ± 8	1.018 (1.015-1.021)	0.000	1.015 (1.012-1.018)	0.000
BMI (kg/m²)	28.0 ± 5.1	28. 0 ± 5.4	0.999 (0.994-1.004)	0.640	--	--
Females	1824 (65)	1972 (67)	0.972 (0.922-1.026)	0.304	--	--
White	1339 (48)	1199 (40)	0.862 (0.818-0.907)	0.000	0.931 (0.883-0.981)	0.007
Living with a partner	1613 (58)	1762 (59)	1.035 (0.983-1.089)	0.189	1.006 (0.959-1.057)	0.796
≥ 8 years of formal education	933 (41)	967 (48)	0.987 (0.932-1.044)	0.646	--	--
Active worker	527 (19)	609 (21)	0.949 (0.893-1.009)	0.094	1.053 (0.989-1.212)	0.109
Ever participate in a diabetes education program**	318 (11)	387 (13)	0.929 (0.865-0.999)	0.047	--	--
Diabetes treatment				0.000	--	--
None	48 (2)	23 (1)				
Diet only	285 (10)	58 (2)	0.522 (0.346-0.786)			
Oral agents	1905 (69)	1390 (47)	1.302 (0.928-1.827)			
Oral agents and insulin	318 (11)	930 (32)	2.300 (1.641-3.224)			
Insulin alone	228 (8)	545 (18)	2.176 (1.551-3.055)			

Insulin use	546 (20)	1475 (50)	1.834 (1.749-1.924)	0.000	1.710 (1.624-1.802)	0.000
SBMG	1,838 (66)	2158 (73)	1.186 (1.118-1.1258)	0.000	1.061(1.001-1.1.23)	0.045
Geographic region				0.000		0.000
North	135 (5)	177 (6)	1.225 (1.073-1.399)		1.137 (0.996-1.298)	
Northeast	814 (29)	1092 (50)	1.212 (1.212-1.365)		1.197 (1.085-1.321)	
Midwest	194 (7)	154 (5)	0.956 (0.842-1.109)		0.858 (0.745-0.989)	
Southeast	1357 (49)	1285 (43)	1.050 (0.951-1.159)		0.959 (0.871-1.056)	
South	291 (10)	251 (8)				

*Poisson Regression adjusted for: age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG and geographic region.
**Data not available for North region (not included in the adjusted analysis)

Table 2. Characteristics of patients with type 2 diabetes according to the five geographic regions of Brazil

	North	Northeast	Midwest	Southeast	South	P
N	312	1906	348	2642	542	-
HbA1c (%)	9.0 ± 2.6	8.9 ± 2.4	8.1 ± 2.0	8.4 ± 2.1	8.3 ± 1.9	<0.01[a]
Age (years)	58 ± 10	61 ± 11	60 ± 11	61 ± 10	62 ± 10	<0.01[bc]
Diabetes duration (years)	10 ± 8	10 ± 8	11 ± 8	11 ± 9	11 ± 9	0.029
BMI (kg/m²)	29.0 ± 5.5	27.2 ± 5.0	27.7 ± 5.2	28.2 ± 5.3	29.1 ± 5.3	<0.01[cde]
Females	193 (62)	1,317 (69)	245 (70)	1,726 (65)	315 (58)	<0.01[f]
White	71 (23)	560 (29)	131 (38)	1,311 (50)	465 (86)	<0.01[f]
Living with a partner	199 (64)	1,099 (58)	185 (53)	1,537 (58)	355 (66)	<0.01[g]
≥ 8 years of formal education	140 (45)	521 (27)	106 (30)	1,011 (38)	122 (27)	<0.01[h]
Active worker	112 (36)	341 (18)	65 (19)	482 (18)	136 (25)	<0.01[i]
Sedentary	134 (43)	670 (35)	147 (43)	1,005 (38)	168 (31)	<0.01[j]
Diabetes treatment						
None	2 (1)	18 (1)	7 (2)	38 (1)	6 (1)	<0.01[f]
Diet only	14 (5)	145 (8)	31 (9)	138 (5)	15 (3)	
Oral agents	172 (59)	1172 (62)	180 (52)	1,426 (54)	345 (64)	
Oral agents and insulin	67 (23)	332 (17)	64 (18)	660 (25)	125 (23)	
Insulin alone	37 (12)	239 (12)	66 (19)	380 (15)	51 (9)	

Data are mean ± SD or number of patients with the characteristic (%)

[a] North and Northeast vs. Midwest, Southeast and South

[b] North vs. Northeast, Southeast and South

[c] Midwest and Southeast vs. South

[d] North vs. Northeast and Center-West

[e] Northeast vs. Southeast and South

[f] Linear-by-linear association

[g] higher in North and South; lower in Midwest

[h] higher in North; lower in Northeast and South

[i] higher in North and South; lower in Northeast and Southeast

[j] higher in North and Midwest; lower in Northeast and South

Table 3. Demographic and clinical characteristics of patients with type 2 diabetes according to ethnicity

	White n = 2538	Non-white n = 3208	P
HbA1c (%)	8.3 ± 2.1	8.8 ± 2.3	<0.01
Age (years)	62 ± 10	60 ± 10	<0.01
Diabetes duration (years)	11 ± 9	11 ± 8	0.06
BMI (kg/m²)	28.2 ± 5.2	27.8 ± 5.3	0.003
Females – n (%)	1,615 (64)	2,178 (68)	<0.01
Living with a partner - n (%)	1,568 (62)	1,805 (56)	<0.01
At least eight years of formal education - n (%)	803 (38)	1,094 (41)	0.011
Active worker - n (%)	520 (21)	616 (19)	0.227
Sedentary – n (%)	904 (36)	1,220 (38)	0.072
Diabetes treatment - n (%)			0.007
None	37 (2)	34 (1)	
Diet only	151 (6)	192 (6)	
Oral agents	1,498 (59)	1,794 (56)	
Oral agents and insulin	533 (21)	714 (22)	
Insulin alone	314 (12)	459 (15)	
Geographic region – n (%)			<0.01
North	71 (23)	241 (77)	
Northeast	560 (29)	1,344 (71)	
Midwest	131 (38)	217 (62)	
Southeast	1,311 (50)	1,329 (50)	
South	465 (86)	77 (14)	

Data are mean ± SD, number of patients with the characteristic (%)

Summary

Article Focus:

Brazil is among the ten countries in the world with the highest prevalence of diabetes mellitus (DM). It is a large country with marked ethnic and socioeconomic differences between regions. Free, universal healthcare coverage is available to all Brazilians, including free access to many drugs. However, status of diabetes control in Brazil is unknown.

Key Messagens:

Patients with type 2 diabetes attending public health care system in Brazil had a mean HbA1c of 8.6%, above recommended international goals. Non-whites and patients living in the Northeast region of the country had the poorest glycemic control. This vulnerable population should receive special attention from government health policies.

Strengths and Limitations

To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil. We used a certified method to analyse HbA1c. However, some limitations were: 1) surveillance was based on self-reported answers, although medical records were consulted when available. 2) Only patients attended by the public heath system were included and 3) lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors.

Supplementary Table. Prevalence of patients characteristics according to HbA1c ≥7%

	HbA1c <7% n = 1520	HbA1c ≥7% n = 4230	PR (CI 95%)	P	Adjusted PR (CI95%)	P
Age (years)	61 ± 11	60 ± 10	0.998 (0.997-1.00)	0.018	0.995 (0.993-0.996)	0.000
Diabetes duration (years)	8 ± 8	12 ± 8	1.013 (1.011-1.015)	0.000	1.010 (1.008-1.012)	0.000
BMI (kg/m²)	28.0 ± 5	28. 0 ± 5	1.001 (0.998-1.004)	0.590	--	--
Females	980 (65)	2816 (67)	1.025 (0.992-1.060)	0.143	--	--
White	752 (50)	1786 (42)	0.925 (0.896-0.955)	0.000	0.948 (0.917-0.979)	0.001
Living with a partner	859 (57)	2516 (60)	1.033 (1.001-1.067)	0.044	1.018(0.993-0.996)	0.987
Active worker	302 (20)	834 (20)	0.997 (0.959-1.037)	0.879	--	--
Insulin use	194 (12)	1827(43)	1.403 (1.364-1.442)	0.000	1.323(1.284-1.363)	0.000
SBMG	965 (64)	3031 (72)	1.112 (1.072-.1.154)	0.000	1.051(1.014-1.089)	0.007
Geographic region				0.000		0.000
North	75 (5)	237 (6)	1.225 (1.073-1.399)		1.119 (0.938-1.106)	
Northeast	438 (29)	1468 (34)	1.212 (1.212-1.365)		1.041 (0.982-1.003)	
Midwest	125 (8)	223 (5)	0.956 (0.842-1.109)		0.832 (0.760-0.912)	
Southeast	732 (48)	1910 (45)	1.050 (0.951-1.159)		0.951 (0.899-1.006)	
South	150 (10)	392 (9)				

Poisson Regression adjusted for: age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG and geographic region.

Factors Associated with Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System

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There is no additional data available for this manuscript.

Abstract:

Objectives: to describe the clinical profile of Brazilian type 2 diabetic patients attending the public healthcare system and identify factors associated with poor glycemic control.

Design: Cross-sectional study.

Setting: 14 centers in five regions of Brazil, including primary care units and outpatient clinics of University Hospitals.

Participants: Patients with type 2 diabetes attending outpatient clinics of public health care system.

Main Outcome Measured: HbA1c, centrally measured by HPLC (NGSP certified).

Results: A total of 5,750 patients aged 61±10 years, with 11±8 years of diabetes duration (66% female, 56% non-white, BMI: 28.0±5.3 kg/m²) were analyzed. Mean HbA1c was 8.6±2.2%, and median HbA1c was 8.1% (6.9 to 9.9%). HbA1c <7% was observed in only 26% of patients. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast (8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South regions (8.3±1.9%). Using the cutoff value of HbA1c above the median, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)], and being from Midwest region [0.858 (0.745-0.989)] were protective factors, while diabetes duration [1.015 (1.012-1.018)], use of insulin [1.710 (1.624-1.802)], and living in the Northeast region [1.197 (1.085-1.321)] were associated with HbA1c >8%.

Conclusions: The majority of Brazilian type 2 diabetic patients attending the public healthcare system had HbA1c levels above recommended targets. The recognition of Northeast residents and non-white patients as vulnerable populations should guide future policies and actions to prevent and control diabetes.

Introduction

Brazil is among the ten countries with the highest prevalence of diabetes mellitus (DM) in the world – about 7.6% (1,2). Diabetes is the fifth underlying cause of death in Brazil, affecting 2.5% of the population (3). Preliminary results obtained by our group (4) show that only 24% of Brazilian diabetic patients had an HbA1c level below the recommended target (HbA1c <7%; 5), despite the availability of free medical care through the public healthcare system (Sistema Único de Saúde-SUS) (6). Medical assistance–and specific drugs, including metformin, sulphonylureas, and insulin, are provided free of charge across the country through primary care units and specific drugstores. Considering that poor diabetic control is associated with increased mortality in diabetic populations (7), it is important to analyze the possible factors associated with the high levels of HbA1c in the population.

Therefore, the aim of this study was to describe the clinical profile of patients with type 2 diabetes receiving public health care in the five regions of Brazil and identify factors associated with poor glycemic control.

Patients

A cross-sectional study was conducted between February 2006 and April 2011 at SUS outpatient clinics with 7,201 type 1 and type 2 diabetes patients from the North (n = 500; 7%), Northeast (n = 2184; 30%), Midwest (n = 461; 6%), Southeast (n = 3382; 47%), and South (n = 674; 9%) regions of Brazil. The number of patients in each region reflects the regional population density as reported in the 2000 national census (8). A preliminary report describing the characteristics of this patient population, for all regions except the North, has been published (4). Briefly, the current study was designed to obtain a representative sample of type 2 diabetic adult patients living in urban areas of Brazil. A total of 14 centers, located in 12 cities belonging to the five

regions of our country were included. The included cities were the largest in their respective region and nine of them ranked among the most populous municipalities in Brazil. We also considered that the data would be more reliable if they were collected from public health care centers that usually take care of at least three hundreds diabetic patients/month. The protocol was approved by the Ethics Committee at Hospital de Clínicas de Porto Alegre and at each participating center/clinic. All patients provided written informed consent.

In the present study, we report the results for 5,750 type 2 diabetic patients for whom HbA1c values were available. Type 2 diabetes was defined as diabetes diagnosed after 30 years of age without insulin use in the first five years after the diagnosis. Patients were from the North (n = 312; 5%), Northeast (n = 1906, 33%), Midwest (n = 348, 6%), Southeast (n = 2642, 46%), and South (n = 542, 9%) regions.

Assessment of Clinical Characteristics

Information on clinical variables (age, gender, ethnicity, DM duration, body weight, height, physical activity, and medications in use,) was obtained by a standardized questionnaire. Ethnicity was self-reported as white or non-white (black, mixed, or other – including Asian and Native Brazilians). Marital status was categorized as living with or without a partner, and working status as being or not currently employed. Educational status was classified as at least eight years or less than eight years of formal education. DM treatment was classified as none, diet alone, oral agents, oral agents plus insulin, and insulin alone. Frequency of self-blood glucose monitoring (SBGM) and hypoglycemic episodes in the previous year were recorded. BMI was calculated (weight/height^2; kg/m^2). Data were collected in 14 cities representing the 5 regions of Brazil: South (Porto Alegre, Curitiba), Southeast (São Paulo, Cotia,

Campinas, Belo Horizonte, Rio de Janeiro), Midwest (Brasilia, Taguatinga), Northeast (Fortaleza, Recife, Salvador), North (Belém, Manaus).

HbA1c measurements

HbA1c was measured in a central laboratory by an ion-exchange high performance liquid chromatography (HPLC) method (reference range 4.7-6.0%) certified by the National Glycohemoglobin Standardization Program (NGSP) and calibrated to the Diabetes Control and Complications Trial (DCCT) standard.

Statistical Analyses

The five regions were compared in terms of clinical variables and HbA1c results by one-way-ANOVA (with Bonferroni post-hoc test) and chi-square tests. The characteristics of patients were evaluated according to glucose control (median HBA1c), region of origin, and self-reported ethnic background. Prevalence ratio (PR) and 95% confidence interval were obtained by Poisson regression analyses to determine the association of different factors with HbA1c >8% (dependent variable). Adjustment was made taking into account independent variables selected based on their significance on univariate analyses and/or biological relevance (age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG, and geographic region).

Variables were expressed as mean ± SD, number of cases (%) and median (25-75 interquartile intervals). HbA1c was also described as median. Statistical analyses were carried out using SSPS 18.0. P values less than 0.05 (two tailed) were considered significant.

RESULTS

A total of 5,750 patients with type 2 diabetes were included and the main characteristics were: age of 61±10 years, diabetes duration of 11±8 years, and BMI 28.0

±5.3 kg/m^2. Most patients were female (66%), non-white (56%), and lived with a partner (59%). One third (33%) had completed eight years of formal education, 20% were employed and 37% were not physically active. Regarding treatment, 1% did not follow any kind of treatment for diabetes, 6% were on diet alone, 57% were taking oral agents, 22% used oral agents and insulin and 13% insulin alone. Mean HbA1c was 8.6 ±2.2% and median was 8.1% (interquartile range: 6.9 to 9.9%). HbA1c <7% was found in only 26% of the patients.

Since the majority of the included patients had a poor glycemic control we decided to compare the characteristic of patients grouped according to median HbA1c (8.0%). **Table 1** describes clinical characteristics and prevalence ratio [PR (CI95%)] of patients with HbA1c ≥8% and HbA1c<8%. In unadjusted model, patients with HbA1c ≥8% were younger, non-whites, with longer DM duration, more sedentary, mainly from North and Northeast regions and treated more frequently with insulin than patients with HbA1c <8%. After adjustment, DM duration [1.015 (1.012-1.018)], insulin use [1.710 (1.624-1.802)], and being from Northeast region [1.197 (1.085-1.321)] was associated with HbA1c ≥8%. On the other hand, age [0.986 (0.983-0.989)], white ethnicity [0.931 (0.883-0.981)] and living in the Midwest region (using the South region as reference) [0.858 (0.745-0.989)] were protective factors. In order to further explore the variables associated with HbA1c ≥8% we performed stratified analysis according to geographic region, ethnicity and insulin use. A **Supplementary Table** shows unadjusted and adjusted analyses applying the same multivariate model using a cutoff of HbA1c<7%. The differences between the groups of patients with HbA1c <7% and ≥7% did not differ substantially from the results using the cutoff of HbA1c<8%.

The characteristics of the patients stratified by region are described in **Table 2**. Mean HbA1c was higher (P <0.01) in the North (9.0±2.6%) and Northeast

(8.9±2.4%) than in the Midwest (8.1±2.0%), Southeast (8.4±2.1%), and South (8.3±1.9%) regions. Moreover, the five regions differed in all other evaluated characteristics. Patients living in the Northeast had the highest prevalence of non-whites, the lowest BMI, and the highest frequency of employed individuals.

Characteristics of patients according self-reported ethnicity (white and non-white) are described in **Table 3**. Non-white subjects had higher HbA1c values, lower BMI, and more years of formal education than white patients. They were also younger, more often female and single.

Of the 5,750 patients in this study, 35% (2,021 patients) used insulin. Of these, 33% (n = 658) used insulin once daily, 58% (n = 1,154) twice daily, and 9% (n = 189) three times a day or more. Eighty-one percent (n = 1,630) of the insulin users performed SBGM, but only 421 (26%) did it on a daily basis. Patients who performed more frequently SBGM had lower values of HbA1c (at least once daily: 9.3 ± 2.1%) than who did not measure capillary glucose (9.7 ± 2.3%; P = 0.008).

Conclusions

In this study, most patients with type 2 diabetes attending the public healthcare system in Brazil had HbA1c levels above the recommended target, that is, above 7%. Being non-white and from the Northeast, as well as the longer diabetes duration, and insulin use were factors associated with poor metabolic control, whereas age and being from the Midwest were associated with HbA1c <8.0% (median HbA1c level for this population). To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil using a certified method to measure HbA1c. We also may consider that the present study included a representative sample of patients with type 2 diabetes living in the urban areas and attending the public healthcare system in Brazil.

In the current survey we chose to use the cutoff value of HbA1c 8% to compare patients with different glycemic control. The recommended target for HbA1c is below 7%, but it has been recently recommended to individualize the goal of HbA1c (5). Since only 26% of our patients achieved this target, we adopted a more representative cutoff value (median HbA1c value of our study population). Nevertheless, we also performed an analysis using the cutoff of HbA1c<7% and the results did not change.

Diabetes control varies in different countries. In the Unites States of America, mean HbA1c among middle-aged adults was approximately 7.3% (9). Type 2 diabetic patients using oral agents to treat diabetes in seven European countries had similar glycemic control (mean HbA1c 7.2%) (10). However, in the EURIKA (11), a study performed in 12 European countries, only 36.7% of patients with type 2 diabetes achieved the goal of HbA1c <6.5%. In the present study, mean HbA1c (8.6±2.2%) was much higher than that observed in these countries, and only 26% of our patients had HbA1c below the 7.0% goal.

In our study, a broad range of HbA1c levels was also observed across Brazilian regions. The poorer glycemic control observed in the Northeast than the other regions might be explained by a diverse ethnic and economic background. Numerous studies show ethnic disparities in HbA1c values; a meta-analysis has reported that African-Americans had absolute HbA1c values 0.65% higher than non-Hispanic whites (13). According to the Brazilian Geography and Statistics Institute, 23.6% of the population in the North and 28.9% in Northeast are white, vs. 41.7% in the Midwest, 56.7% in the Southeast, and 78.5% in the South (12). In our study, the difference in HbA1c between whites and non-whites was about 0.5%. Regarding the role of economic status, *per capita* income is almost twice as high in the South than in the Northeast (14). In this sense, a European surveillance of socio-economic predictors of mortality has

demonstrated an association between low income (15) and higher mortality in type 2 diabetic males.

Free, universal health care has been available to all Brazilian citizens since 1988 (6), including free access to many drugs. Metformin, sulphonylureas, and insulin are distributed in primary care units and drugstores around the country. However, other medications used to treat diabetes are not covered. Also, SBGM devices are not freely supplied. Therefore, although our Public Health System may represent an advance in health care, it has not been enough to reach glycemic control targets in diabetes care. Other measures are highly necessary, and should include a structured diabetes education program (16), public policies to improve adherence to diet and exercise, and free access to SBGM, at least to all patients on insulin (5).

The present study has limitations. Firstly, surveillance was based on self-reported answers, although medical records were consulted when available. Moreover, only patients attending the public healthcare system were evaluated. It is known that almost one fourth of the Brazilian population rely on private healthcare (17). Lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors. It is also important to remember that reverse causality is always possible in cross-sectional studies, and poor glycemic control in patients using insulin cannot be attributed to insulin prescription *per se*. Because insulin is generally prescribed to patients with more severe diabetes, the health status of these patients may also account for their poor glycemic control. We may consider that had included only diabetic patients living in urban areas could represent a potential limitation. However we can speculate that patients from the rural areas of our country, who attend primary care units less equipped and with less trained health care personal, may have even a poorer diabetes control.

In conclusion, Brazilian patients with type 2 diabetes attending the public healthcare system have poor glycemic control as demonstrated by HbA1c values far above the recommended target. New strategies are necessary to improve glycemic control in this population. Furthermore, the increased vulnerability of Northeast residents and non-white patients to poor metabolic control should be taken into account when designing strategies to control diabetes.

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Table 1 . Prevalence of patients characteristics according to HbA1c ≥8%

	HbA1c <8% n = 2791	HbA1c ≥8% n = 2959	PR (CI 95%)	P	Adjusted PR (CI95%) *	P
Age (years)	62 ± 11	60 ± 10	0.991 (0.989-0.993)	0.000	0.986 (0.983-0.989)	0.000
Diabetes duration (years)	9 ± 8	12 ± 8	1.018 (1.015-1.021)	0.000	1.015 (1.012-1.018)	0.000
BMI (kg/m²)	28.0 ± 5.1	28. 0 ± 5.4	0.999 (0.994-1.004)	0.640	--	--
Females	1824 (65)	1972 (67)	0.972 (0.922-1.026)	0.304	--	--
White	1339 (48)	1199 (40)	0.862 (0.818-0.907)	0.000	0.931 (0.883-0.981)	0.007
Living with a partner	1613 (58)	1762 (59)	1.035 (0.983-1.089)	0.189	1.006 (0.959-1.057)	0.796
≥ 8 years of formal education	933 (41)	967 (48)	0.987 (0.932-1.044)	0.646	--	--
Active worker	527 (19)	609 (21)	0.949 (0.893-1.009)	0.094	1.053 (0.989-1.212)	0.109
Ever participate in a diabetes education program**	318 (11)	387 (13)	0.929 (0.865-0.999)	0.047	--	--
Diabetes treatment				0.000	--	--
None	48 (2)	23 (1)				
Diet only	285 (10)	58 (2)	0.522 (0.346-0.786)			
Oral agents	1905 (69)	1390 (47)	1.302 (0.928-1.827)			
Oral agents and insulin	318 (11)	930 (32)	2.300 (1.641-3.224)			
Insulin alone	228 (8)	545 (18)	2.176 (1.551-3.055)			

Insulin use	546 (20)	1475 (50)	1.834 (1.749-1.924)	0.000	1.710 (1.624-1.802)	0.000
SBMG	1,838 (66)	2158 (73)	1.186 (1.118-1.1258)	0.000	1.061(1.001-1.1.23)	0.045
Geographic region				0.000		0.000
North	135 (5)	177 (6)	1.225 (1.073-1.399)		1.137 (0.996-1.298)	
Northeast	814 (29)	1092 (50)	1.212 (1.212-1.365)		1.197 (1.085-1.321)	
Midwest	194 (7)	154 (5)	0.956 (0.842-1.109)		0.858 (0.745-0.989)	
Southeast	1357 (49)	1285 (43)	1.050 (0.951-1.159)		0.959 (0.871-1.056)	
South	291 (10)	251 (8)				

*Poisson Regression adjusted for: age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG and geographic region.
**Data not available for North region (not included in the adjusted analysis)

Table 2. Characteristics of patients with type 2 diabetes according to the five geographic regions of Brazil

	North	Northeast	Midwest	Southeast	South	P
N	312	1906	348	2642	542	-
HbA1c (%)	9.0 ± 2.6	8.9 ± 2.4	8.1 ± 2.0	8.4 ± 2.1	8.3 ± 1.9	<0.01[a]
Age (years)	58 ± 10	61 ± 11	60 ± 11	61 ± 10	62 ± 10	<0.01[bc]
Diabetes duration (years)	10 ± 8	10 ± 8	11 ± 8	11 ± 9	11 ± 9	0.029
BMI (kg/m²)	29.0 ± 5.5	27.2 ± 5.0	27.7 ± 5.2	28.2 ± 5.3	29.1 ± 5.3	<0.01[cde]
Females	193 (62)	1,317 (69)	245 (70)	1,726 (65)	315 (58)	<0.01[f]
White	71 (23)	560 (29)	131 (38)	1,311 (50)	465 (86)	<0.01[f]
Living with a partner	199 (64)	1,099 (58)	185 (53)	1,537 (58)	355 (66)	<0.01[g]
≥ 8 years of formal education	140 (45)	521 (27)	106 (30)	1,011 (38)	122 (27)	<0.01[h]
Active worker	112 (36)	341 (18)	65 (19)	482 (18)	136 (25)	<0.01[i]
Sedentary	134 (43)	670 (35)	147 (43)	1,005 (38)	168 (31)	<0.01[j]
Diabetes treatment						
None	2 (1)	18 (1)	7 (2)	38 (1)	6 (1)	<0.01[f]
Diet only	14 (5)	145 (8)	31 (9)	138 (5)	15 (3)	
Oral agents	172 (59)	1172 (62)	180 (52)	1,426 (54)	345 (64)	
Oral agents and insulin	67 (23)	332 (17)	64 (18)	660 (25)	125 (23)	
Insulin alone	37 (12)	239 (12)	66 (19)	380 (15)	51 (9)	

Data are mean ± SD or number of patients with the characteristic (%)

[a] North and Northeast vs. Midwest, Southeast and South

[b] North vs. Northeast, Southeast and South

[c] Midwest and Southeast vs. South

[d] North vs. Northeast and Center-West

[e] Northeast vs. Southeast and South

[f] Linear-by-linear association

[g] higher in North and South; lower in Midwest

[h] higher in North; lower in Northeast and South

[i] higher in North and South; lower in Northeast and Southeast

[j] higher in North and Midwest; lower in Northeast and South

Table 3. Demographic and clinical characteristics of patients with type 2 diabetes according to ethnicity

	White n = 2538	Non-white n = 3208	P
HbA1c (%)	8.3 ± 2.1	8.8 ± 2.3	<0.01
Age (years)	62 ± 10	60 ± 10	<0.01
Diabetes duration (years)	11 ± 9	11 ± 8	0.06
BMI (kg/m²)	28.2 ± 5.2	27.8 ± 5.3	0.003
Females – n (%)	1,615 (64)	2,178 (68)	<0.01
Living with a partner - n (%)	1,568 (62)	1,805 (56)	<0.01
At least eight years of formal education - n (%)	803 (38)	1,094 (41)	0.011
Active worker - n (%)	520 (21)	616 (19)	0.227
Sedentary – n (%)	904 (36)	1,220 (38)	0.072
Diabetes treatment - n (%)			0.007
None	37 (2)	34 (1)	
Diet only	151 (6)	192 (6)	
Oral agents	1,498 (59)	1,794 (56)	
Oral agents and insulin	533 (21)	714 (22)	
Insulin alone	314 (12)	459 (15)	
Geographic region – n (%)			<0.01
North	71 (23)	241 (77)	
Northeast	560 (29)	1,344 (71)	
Midwest	131 (38)	217 (62)	
Southeast	1,311 (50)	1,329 (50)	
South	465 (86)	77 (14)	

Data are mean ± SD, number of patients with the characteristic (%)

Summary

Article Focus:

Brazil is among the ten countries in the world with the highest prevalence of diabetes mellitus (DM). It is a large country with marked ethnic and socioeconomic differences between regions. Free, universal healthcare coverage is available to all Brazilians, including free access to many drugs. However, status of diabetes control in Brazil is unknown.

Key Messagens:

Patients with type 2 diabetes attending public health care system in Brazil had a mean HbA1c of 8.6%, above recommended international goals. Non-whites and patients living in the Northeast region of the country had the poorest glycemic control. This vulnerable population should receive special attention from government health policies.

Strengths and Limitations

To the best of our knowledge, this is the largest surveillance study to assess glycemic control in Brazil. We used a certified method to analyse HbA1c. However, some limitations were: 1) surveillance was based on self-reported answers, although medical records were consulted when available. 2) Only patients attended by the public heath system were included and 3) lastly, due to its cross-sectional design, our study was able to identify associations between several factors and glycemic control, but was unable to pinpoint risk factors.

Supplementary Table. Prevalence of patients characteristics according to HbA1c ≥7%

	HbA1c <7% n = 1520	HbA1c ≥7% n = 4230	PR (CI 95%)	P	Adjusted PR (CI95%)	P
Age (years)	61 ± 11	60 ± 10	0.998 (0.997-1.00)	0.018	0.995 (0.993-0.996)	0.000
Diabetes duration (years)	8 ± 8	12 ± 8	1.013 (1.011-1.015)	0.000	1.010 (1.008-1.012)	0.000
BMI (kg/m²)	28.0 ± 5	28. 0 ± 5	1.001 (0.998-1.004)	0.590	--	--
Females	980 (65)	2816 (67)	1.025 (0.992-1.060)	0.143	--	--
White	752 (50)	1786 (42)	0.925 (0.896-0.955)	0.000	0.948 (0.917-0.979)	0.001
Living with a partner	859 (57)	2516 (60)	1.033 (1.001-1.067)	0.044	1.018(0.993-0.996)	0.987
Active worker	302 (20)	834 (20)	0.997 (0.959-1.037)	0.879	--	--
Insulin use	194 (12)	1827(43)	1.403 (1.364-1.442)	0.000	1.323(1.284-1.363)	0.000
SBMG	965 (64)	3031 (72)	1.112 (1.072-.1.154)	0.000	1.051(1.014-1.089)	0.007
Geographic region				0.000		0.000
North	75 (5)	237 (6)	1.225 (1.073-1.399)		1.119 (0.938-1.106)	
Northeast	438 (29)	1468 (34)	1.212 (1.212-1.365)		1.041 (0.982-1.003)	
Midwest	125 (8)	223 (5)	0.956 (0.842-1.109)		0.832 (0.760-0.912)	
Southeast	732 (48)	1910 (45)	1.050 (0.951-1.159)		0.951 (0.899-1.006)	
South	150 (10)	392 (9)				

Poisson Regression adjusted for: age, diabetes duration, ethnicity, living with partner, working status, insulin use, SBMG and geographic region.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract OK
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found OK
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported OK
Objectives	3	State specific objectives, including any prespecified hypotheses OK
Methods		
Study design	4	Present key elements of study design early in the paper OK
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection OK
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants OK
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group OK
Bias	9	Describe any efforts to address potential sources of bias OK
Study size	10	Explain how the study size was arrived at OK
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why OK
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding OK
		(*b*) Describe any methods used to examine subgroups and interactions OK
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed OK
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders OK
		(b) Indicate number of participants with missing data for each variable of interest OK
Outcome data	15*	Report numbers of outcome events or summary measures OK
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and

		their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included OK
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives OK
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias OK
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence OK
Generalisability	21	Discuss the generalisability (external validity) of the study results OK
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based OK

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

ANSWER TO MANAGING EDITOR COMMENTS

1) Please use the title to frame the research question, rather than headline the results.

Answer: Thank you for the suggestion. We think that the new title: "Factors Associated with Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System" meets your comment.

ANSWER TO REVIEWERS

Answer to ProfessorChing Chiu

1) This is a cross-sectional survey of blood glucose control in a cohort of 5,750 Brazilian type 2 diabetic patients attending the public healthcare system. The data is interesting and could be of clinical and public health significance. Reviewer has some suggestions below.

Answer: Thank you for your comments. The answers are described below**.**

2) The American Diabetes Association recommends that the HbA1c should be below 53 mmol/mol (7.0%) for most patients. In page 7, line 2 of the manuscript, authors also stated that HbA1c <7% was found in only 26% of their patients. However, in Table 1 8% (the median for this cohort) was used as a cutoff point for the analysis. Reviewer thinks that using 7% as the cutoff is more clinically relevant and easy for comparison with other studies.

Answer: Thank you for this observation. We agree that usually the recommended target for HbA1c is below 7%. However, only 26% of your patients obtained HbA1c<7% and this aspect could have limited the statistical analyses. By using the median we obtained a more balanced distribution of the factors between the groups. Moreover, recently the American Diabetes Association considered that the goal of HbA1c should be individualized taking into account, among others, age, diabetes duration and presence of complications. So, in this context, we considered that the adopted cutoff value of HbA1c 8% adequate for our population with 61 ± 10 years old with diabetes duration of 11± 4 years. Nevertheless, we performed an analysis using the suggested cutoff and the results did not change substantially. A supplementary table using HbA1c≥7% was included in the manuscript. These comments were added to the conclusion section.

3) It is unclear that what confounders were adjusted in the Poisson regression (page 6, lines 18-28 and Table 1). Authors should clearly list them.

Answer: Poisson regression was adjusted for: age, diabetes, ethnicity, living with partner, working status, insulin use, SBMG, and geographic region. Adjustments for were included in the table 1.

4) Figure 1 was not referred in the text and is redundant with Table 2.

Answer: Thank you for your cautious revision. Figure 1 was deleted.

5) Authors should double check their numbers throughout the manuscript. There are some errors, for example in Table 2: the percentage for over 8 years of education in Northeast should be 27% but not 34%.

Answer: Thank you for careful review. We double checked the numbers of manuscript and we think they are now correct.

Answer to Professor John A McKnight

1) This is a nice study, well written and very clear. The main problem is selection of the population studied. This needs to be more clearly defined to enable interpretation of the results. The population of Brazil is very large, yet the authors describe results for around 5000 patients with diabetes, a very small proportion of the Brazilian diabetic population. Have they studied a group that is really representative? If this issue is clearly addressed I would be delighted to support publication of this work

Answer: Thank you for your comments. This is a very important aspect and we would like to thank you for the opportunity to expand the rational of this study. The main objective of our study was to estimate the proportion of diabetic patients who needed to improve their metabolic control, which factors were associated with poor glycemic control, and to fundament government policies to implement strategies to improve diabetes care in the public healthcare system.

There are very few previous cohort and/or epidemiological studies in type 2 diabetes in Brazil. Some studies had included selected patients, such as those with some diabetic complications such as microalbuminuria (1,2) or microvascular or macrovascular complications (3), or evaluated specific ethnic groups (4). We identified only one study with a relatively unselected sample. That study assessed the prevalence of diabetes in the urban adult Brazilian population. It was a multicenter, cross-sectional

survey in a random sample of individuals from nine large cities (5). Please find in the table below the main characteristics of the present study and the prevalence study.

	Present study	Marlebi DA, Franco LJ 1992
n	5750	2294
Age (years)	61 ± 10	30-69
Female Sex	66.0%	64.7%
White ethnicity	44%	67.4%
DM duration (years)	11 ± 8.0	--
BMI (kg/m^2)	28.0 ± 5.3	--
HbA1c (%)	8.6 ± 2.2	--

The main demographic characteristics of both sample of patients seems to be similar except by a higher prevalence of white subjects in the study of Malerby and Franco. However, the proportion of white subjects in our study reflects more the proportion of white individuals in Brazilian urban areas, 50% according the 2010 Census (Brazilian Institute of Geography and Statistics - IBGE, Instituto Brasileiro de Geografia e Estatística). Therefore we may consider that our sample is representative of diabetic patients in Brazil.

Moreover, we also calculated the sample size needed to estimate the prevalence of the adequate glycemic control based on the information that about 27% (range from 22% to 31%) (*assumed rate*) of type 2 diabetic patients in Brazil have an adequate glycemic control (data obtained from Social Security Health Minister). Considering an acceptable difference of 3% (half of the total width of the desired confidence interval of prevalence values of adequate glycemic control) the required number of patients was 1051 (alpha of 0·05; predicted subject loss of 20%; WinPepi, version 11.32 program). Besides this calculation, we included 5750 patients in order to be possible to evaluate each geographic region of Brazil. The sample size for each region was based, as close as possible, on the relative region distribution of population according to the Brazilian Institute of Geography and Statistics (IBGE, Instituto Brasileiro de Geografia e Estatística, Census 2000). We also considered that the data would be more reliable if they were collected from public health care centers that usually take care of at least

three hundreds patients/month. So, we identified 14 centers located in the 12 most populous cities distributed along the five regions of Brazil. The table below shows the official distribution of Brazilian population in the five regions and the size of studied sample according each region.

Brazilian Regions	Proportion of the population in each region considering total Brazilian population	Patients included n (%)
Total	100%	5750
North	7,9%	312 (5,4%)
Northest	28,0%	1906 (33,1%)
Southest	42,3%	2642 (45,9%)
South	14,5%	542 (9,4%)
Midwest	7,2%	348 (6,1%)

In conclusion, we may consider that the sample of diabetic patients included is representative of diabetes population living in urban centers. We can speculate that patients living in the rural areas of our country, who attend primary care units less equipped and with less trained health care personal, may have even a poorer diabetes control. Comments were added in the text in the Patients and Discussion sections.

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1) Viana LV, Gross JL, Camargo JL, Zelmanovitz T, da Costa Rocha EP, Azevedo MJ. Prediction of cardiovascular events, diabetic nephropathy, and mortality by albumin concentration in a spot urine sample in patients with type 2 diabetes. J Diabetes Complications. **2012 5**:407-12

2) Murussi M, Campagnolo N, Beck MO, Gross JL, Silveiro SP. High-normal levels of albuminuria predict the development of micro- and macroalbuminuria and increased mortality in Brazilian Type 2 diabetic patients: an 8-year follow-up study. Diabet Med. **2007 10**:1136-42.

3) Cardoso CR, Ferreira MT, Leite NC, Salles GF. Prognostic Impact of Aortic Stiffness in High-Risk Type 2 Diabetic Patients: The Rio de Janeiro Type 2 Diabetes Cohort Study. Diabetes Care 2013 Jul 22 [Epub ahead of print].

4) Gimeno SG, Ferreira SR, Franco LJ, Hirai AT, Matsumura L, Moisés RS. Prevalence and 7-year incidence of Type II diabetes mellitus in a Japanese-Brazilian population: an alarming public health problem. Diabetologia **2002 12**:1635-8

5) Malerbi DA, Franco LJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in the urban Brazilian population aged 30-69 yr. The Brazilian Cooperative Group on the Study of Diabetes Prevalence. Diabetes Care 1992 11:1509-16.